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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,242	FAGAN ET AL.	
	Examiner	Art Unit	
	Sharon Wen	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-72* is/are pending in the application.

4a) Of the above claim(s) *47-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *46,71 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: sequence alignment sheets attached.

DETAILED ACTION

1. The Art Unit location of the examiner of this application in the PTO has changed. To aid in the correlating any papers for this application, all further correspondence regarding this application should be directed to Sharon Wen, Group Art Unit **1644**, Technology Center 1600.

Election/Restrictions

2. Applicant's election of Group I, claims 46 and 71-72, in the Response to Election / Restriction filed on 07/27/2007 is acknowledged. Because Applicant did no distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. See MPEP § 818.03(a).

3. Claims 46-72 are pending.

Claims 46(b-h, k-o) and 47-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic claim.

Claims 46(a, i-j) and 71-72 are currently under examination as they read on a composition of matter comprising an isolated polypeptide, a pharmaceutical composition, and a vaccine composition.

Applicant is invited to amend the claims, especially claim 46, to recite the elected species.

Priority

4. The effective priority date for claims 46(a, i-j) and 71-72 is deemed to be the filing date of PCT/GB03/04786 i.e. 11/07/2003.

Specification

5. Applicant is requested to review the application for the use of trademarks, embedded hyperlinks and/or other form of browser-executable code.

Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference.

Information Disclosure Statement

6. Applicant's IDS, filed 05/11/2007, is acknowledged, and has been considered.

Claim Rejections - 35 USC § 112 second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 46(a, i-j) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim is indefinite for being in improper Markush format. The Office recommends the use of the phrase "**selected from the group consisting of**..." with the use of the conjunction "**and**" rather than "or" in listing the species. See MPEP 2173.05(h).

Currently, there appears to be missing the word "and" between subclauses (10) and (11) of claim 46(a).

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any New Matter. See MPEP § 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 46(a, i-j) and 71-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **written description** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C § 112, paragraph 1 "Written Description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January, 2001, See especially page 1106 3rd column).

Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for the genus of:

a) **fragments** of an alpha-2-macroglobulin-like proteinase inhibitor wherein the fragments comprises or consists, has greater than 80% sequence identity with, has an antigenic determinant in common with or consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO: 68, 70 or 72; **OR**

b) **functional equivalents** of an alpha-2-macroglobulin-like proteinase inhibitor wherein the functional equivalent is a homologous of, has greater than 80% sequence identity with, exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO: 68, 70 or 72.

Fragments

The claims recite a genus of **fragments** of an alpha-2-macroglobulin-like proteinase inhibitor wherein the fragments comprises or consists, has greater than 80% sequence identity with, has an antigenic determinant in common with or consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO: 68, 70 or 72, but do not require that the fragments share any alpha-2-macroglobulin-like proteinase inhibitor activity, a feature deemed essential to the instant invention. In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Functional equivalent

The claim recites a genus **functional equivalents** of an alpha-2-macroglobulin-like proteinase inhibitor wherein the functional equivalent is a homologous of, has greater than 80% sequence identity with, exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO: 68, 70 or 72, but the specification failed to support all the possible functional equivalents. The fact that two polypeptides that are homologous in structure or share certain degrees of identity in sequence does not in and of itself required that the two sequences share any functional activity such as alpha-2-macroglobulin-like proteinase inhibitor activity. In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Comprising/has

Furthermore, the term "**comprising**" or "**has**" in the instant claims are open-ended and extend the polypeptide to include additional non-disclosed sequences on either or both sides of the disclosed region. As the term "comprising" or "has" is applied to sequences other than full length SEQ ID NO: 68, 70 or 72, there does not appear to be sufficient written description in the specification as filed to convey to the skilled artisan that the inventors, at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

11. Claim 46(j) is further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claim is directed to an isolated polypeptide of SEQ ID NO: 68, 70 or 72 or functional equivalent or fragment thereof and a **vaccine** comprising said polypeptide or functional equivalent or fragment thereof. Applicant does not appear to have provided sufficient teaching on the immunogenic capacity of the polypeptide nor sufficient *in vivo* data on the efficacy of the **vaccine**. Applicant alleges that the polypeptide of the invention can be used in vaccines to raise antibodies and the vaccine comprising the polypeptide may be prophylactic (i.e. to prevent infection) or therapeutic (i.e. to treat disease after infection) (see page 44 of specification); however there does not appear to be any in the specification to indicate that an antibody to the polypeptide would be produced in host organism. Furthermore, it is unpredictable whether the raised antibody would be immunoprotective in host organisms. It is therefore considered that the claims to a vaccine comprising the polypeptides of SEQ ID NO: 68, 70 and 72, and functional equivalents and fragments thereof are inoperative.

Furthermore, there is insufficient evidence provided the claimed method and composition induces protective immunity against any alpha-2-macroglobulin-like proteinase inhibitor, as a "disease causing agent" (see specification, page 44 lines 25-28). For example, it is unclear from the specification that the disclosed polypeptide elicit a level of cellular and/or humoral immunity able to prevent and protect an individual against challenge with various pathological diseases disclosed by Applicant including cell proliferative disorders (e.g., neoplasm), autoimmune diseases (arthritis), neurological disorders (e.g., Alzheimer's disease), metabolic disorders (diabetes mellitus) and infectious diseases (e.g., AIDS), (see page 13 of specification and claim 55). One of skill in the art is well aware that vaccine development for Alzheimer's disease (AD) is highly unpredictable. In this regard, DaSilva et al. teach that "a definitive diagnosis of Alzheimer's disease can only be made by post-mortem examination of the brain" (*Current Pharmaceutical Design*, 2006, 12:4283-4293, see entire document, in particular, see page 4283, left column, second paragraph), thus therapy can only be initiated in patients with established

AD pathology, making prevention of the onset of AD, as encompassed by the vaccine claim in the present invention, virtually impossible.

In view of the unpredictability taught by DaSilva et al. as stated above, the skilled artisan would not reasonably expect a generically recited composition comprising the polypeptide of SEQ ID NO: 68, 70 or 72 or functional equivalent or fragment thereof to prevent various diseases broadly encompassed by the present vaccine claims. Thus the recitation of the claim language does not allow the skilled artisan to make and use the polypeptide commensurate in scope with the instant claims without undue experimentation.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 46(a, i-j) and 71 are rejected under 35 U.S.C. 102(a) as being anticipated by Kekuda et al. (US 2004/0002120 A1, see entire document) and as evidenced by the sequence alignment attached to this Office Action and the instant specification.

Keduda et al. teach an isolated polypeptide (SEQ ID NO: 124), and fragment thereof, comprising an amino acid sequence greater than 80% identity with SEQ ID NO: 68 of the present application (see sequence alignment and claims 1-4). Given the present claim construction and the disclosure by the instant specification (see pages 18-20 of the specification), the prior art polypeptide reads on a fragment and a function equivalent of SEQ ID NO: 68.

In addition, Keduda et al. teach a pharmaceutical composition comprising the polypeptide (see claim 5).

For examination purposes, given that the recitation of "vaccine" in claim 46(j) merely comprises a known composition, the term carries little patentable weight absent evidence of structural difference from a pharmaceutical composition as taught by the prior art.

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

14. Claims 46(a, i-j) and 71-72 are rejected under 35 U.S.C. 102(a)(e) as being anticipated by Rosen et al. (US 2003/0044890 A1, see entire document) and as evidenced by the sequence alignment attached to this Office Action.

Rosen et al. teach a polypeptide (SEQ ID NO: 19), and fragment thereof, comprising an amino acid sequence greater than 80% identity with SEQ ID NOs: 70 and 72 of the present application (see sequence alignment and claims 11). Given the present claim construction and the disclosure by the instant specification (see pages 18-20 of the specification), the prior art polypeptide reads on a fragment and a function equivalent of SEQ ID NO: 70 or 72.

In addition, Rosen et al. teach a pharmaceutical and vaccine compositions comprising the polypeptide (see paragraphs [0322], [0510] and [0727]).

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Wen whose telephone number is (571) 270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Wen Ph.D.
Patent Examiner
August 27, 2007

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8/28/07